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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,748	03/26/2001	Steven M. Tracy	UNMC 63116-CIP/13292-0004	7857

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	16

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,748	TRACY, STEVEN M.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-26,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-26 and 28-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The requirement for a substitute Declaration is withdrawn in view of applicants' remarks filed 3/25/03.

Applicants' amendment has obviated the 35 USC 112, 2nd paragraph rejection of claim 18.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-26 and 28-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained for reasons of record in the previous Office Action (Paper #14) and for reasons outlined below.

Applicants' traverse this rejection by asserting that the claimed invention must be taken as in compliance with the enabling requirement of 35 USC 112, 1st paragraph unless there is reason to doubt the objective truth of the statements contained within the application.

Applicant's arguments filed 3/25/03 have been fully considered but they are not persuasive. It is noted that the examiner has not doubted the objective truth of the

instant disclosure. What the examiner has done is applied the review standards (analysis of the *Wands* factors) that the courts have determined are essential for determining whether a claimed invention is enabled. An analysis of the *Wands* factors resulted in a conclusion that the skilled artisan would have needed to have conducted undue and excessive experimentation in order to practice the claimed invention.

Applicants assert that the claimed compositions are designed for *in vivo* use in therapeutic applications in humans **and** as research tools to elucidate the biochemical and physiological basis for IDDM in non-human animals (e.g. NOD mice). Applicants assert that these two utilities are enabled by the specification and that the specification provides two working examples of the utility of the claimed compositions using the NOD mouse model of IDDM.

In response, the examiner notes that applicants' arguments with regard to the utilities of the instant invention appear to be directed to overcoming a utility rejection. The utility of the claimed invention has never been in question and arguments directed to the utility of the invention are not on point here. With regard to the two "working examples" applicants assert are provided in the instant specification, it is worthwhile to examine what applicants are actually claiming. The instant pending claims recite a composition for "treating an **individual** for insulin-dependent diabetes mellitus" and a method for "treating, preventing or suppressing onset of insulin-dependent diabetes mellitus in an **individual**". An examination of the specification indicates that the "individual" referred to in the claims reads on a human, not a mouse. Therefore, applicants' examples using an artificial mouse model system (NOD mice) cannot be

considered to be a working example of the **claimed invention**. Applicants provide only one disclosed use for the claimed compositions, that is, for the treatment or suppression of IDDM in individuals and for suppressing the onset of IDDM in individuals. Applicants do not disclose, in the instant application, that the instant invention can be used as a research tool for study of the biochemical and physiological basis for IDDM in mouse model systems.

Applicants assert that the data they present in the NOD mouse model are applicable to humans because the NOD model has been used for over 20 years and is "as good as it gets", short of study in humans, for assessing preclinical evaluation of agents against IDDM. Applicants assert that the data they present in the specification show that coxsackievirus vectors expressing IL-4 protects mice against IDDM and that inoculation of juveniles with coxsackieviruses suppresses the onset of IDDM and that this conclusion is supported by Tracy et al., J. Virol., Vol. 76, 2002, pp. 12097-12111. Several references are cited concerning the use of the NOD mouse model.

In response, the examiner notes that the art dealing with the NOD mouse system does not apparently indicate that results obtained using this model are art recognized by those of skill in the art as being predictive of results which would be obtained in humans. Indeed, the Atkinson et al. reference (cited by applicants) indicates that the differences between the NOD mice and humans with regard to IDDM restrict the interpretation of results obtained using this model (paragraph bridging pp. 601-602) and that "It is clear that the genus-unique and strain-specific aspects of diabetogenesis in NOD mice must be fully understood and appreciated if we are to know which

therapeutic protocols are reasonable to extrapolate to humans and which are not." (p. 603, right column) and that "...exploitation of the peculiarities of the NOD genome for clinical research is yet to be fully realized." (p. 604) and that:

> It is clear that the course of type I diabetes development in randomly breeding humans will not be as easily deviated as it is in highly inbred rodent models in which genetic risk is a constant such that interventions can be initiated at very early stages of pathogenesis. Thus no investigator should assume that the available mouse and rat models spontaneously developing type I diabetes represent complete surrogates for humans. (p. 604).

The Tracy et al. reference (cited by applicants) notes that "...there is no consensus as to the etiologic role for CVB in T1D development..." (p. 1) and that "The mechanisms underlying the onset of T1D are not clearly understood." (p. 10) and that "Although not disproven, support for a hypothetical role for CVB in the causation of diabetes is certainly much weaker than that available on the etiologic role of CVB in human myocarditis and pancreatitis." (p. 10) and that:

> Understanding that the NOD mouse remains only a model of human T1D, we nonetheless suggest that the consistent and marked suppression of T1D in the inbred, genetically T1D-prone NOD mice by all CVB strains used in the present study is an encouraging finding, **one that suggests that it may be possible one day to induce CVB vaccine-mediated suppression of T1D in the genetically outbred human population** (emphasis added)." (p. 13).

The above statement by Tracy et al. (published more than a year after the effective filing date of the instant application) indicating that some day it may be possible to use CVB as a vaccine to suppress T1D in humans is hardly evidence that the skilled artisan would only have to conduct routine experimentation to practice the claimed invention. Indeed, from a review of the art, it appears that the instant invention is based upon a

controversial hypothesis concerning the involvement of CVB infection in the induction of IDDM in humans.

Finally, applicants assert that while the examiner has asserted that the IDDM and gene therapy arts are unpredictable, these statements carry little weight in view of the specification's *in vivo* proof of efficacy in the NOD mouse model system. Applicants indicate that to require additional evidence would require human clinical data which is beyond the scope of the enablement requirement.

In response, the examiner notes that the deficiencies in the NOD model, with regard to extrapolating results obtained therein to results which the skilled artisan would reasonably expect to see in humans, are discussed above and in the references supplied by applicants in the instant response. The examiner is not requiring human clinical data. Any data will be considered as evidence of enablement; however, the data must be such that the skilled artisan would conclude that the results obtained could be extrapolated to humans with a reasonable degree of success and predictability. There must be an art recognized (or disclosed) correlation between the results obtained using the model system and the results which the skilled artisan would reasonable expect to see in humans. In the instant case, give that the disease condition (IDDM) to be treated or prevented is poorly understood, the hypothesis concerning involvement of CVB infection in the etiology of IDDM is controversial at best and the model system used to generate data in support of the instant invention (NOD mice) has significant drawbacks with regard to extrapolation of results to humans, it must be considered that the skilled

artisan, attempting to practice the claimed invention, would have to have practiced excessive and undue experimentation.

The claims therefore stand rejected.

No Claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
June 9, 2003

DAVID GUZO
PRIMARY EXAMINER